## (FILE 'HOME' ENTERED AT 17:37:50 ON 20 JUN 2000) FILE 'MEDLINE, BIOSIS, CAPLUS, USPATFULL' ENTERED AT 17:38:38 ON 20 JUN 2000 8621 S NEUROECTODERM? L1 L2 1342108 S ANTIBODY OR ANTIBODIES L3 56 S CHLOROTOXIN? L48267 S CHLORIDE CHANNEL L5 2525715 S TUMOR? OR CANCER? OR NEOPLAS? 20 S L3 AND L4 L6 454 S L2 AND L4 L7 9 S L6 AND L5 L8 L9 108 S L7 AND L5 => dup rem 18 PROCESSING COMPLETED FOR L8 6 DUP REM L8 (3 DUPLICATES REMOVED) => d 110 1-6 bib abs L10 ANSWER 1 OF 6 USPATFULL 2000:21668 USPATFULL AN TIMethod of diagnosing and treating gliomas IN Ullrich, Nicole, Fairfield, CT, United States Sontheimer, Harald W., Birmingham, AL, United States UAB Research Foundation, Birmingham, AL, United States (U.S. PΑ corporation) PΙ US 6028174 20000222 US 1997-980388 19971128 (8) ΑI RLI Division of Ser. No. US 1996-774154, filed on 26 Dec 1996 US 1995-9283 19951227 (60) PRAT $\mathbf{DT}$ Utility EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Sun-Hoffman, Lin Adler, Benjamin Aaron LREP CLMN Number of Claims: 3 ECLExemplary Claim: 1 20 Drawing Figure(s); 20 Drawing Page(s) DRWN LN.CNT 1434 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The present invention provides a recombinant toxin and monoclonal antibody which specifically binds to glial-derived or meningioma-derived tumor cells. Also provided are various methods of screening for malignant gliomas and meningiomas. Further provided are methods of treating malignant gliomas, including glioblastoma multiforme and astrocytomas. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 2 OF 6 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1 T<sub>1</sub>1.0 1999:330028 CAPLUS ΑN 130:335024 DN ΤI Method of diagnosing and treating gliomas

Ullrich, Nicole; Sontheimer, Harald W.

UAB Research Foundation, USA

U.S., 34 pp.

IN

PΑ

SO

CODEN: USXXAM DT Patent LA English

PRAI US 1995-9283 19951227 US 1996-774154 19961226

AB The present invention provides a recombinant toxin and monoclonal antibody

which specifically binds to glial-derived or meningioma-derived tumor cells. Also provided are various methods of screening for malignant gliomas and meningiomas. Further provided are methods of treating malignant gliomas, including glioblastoma multiforme and astrocytomas.

RE.CNT 2

RE

- (1) Ullrich; Am J Physiol 1996, V270(5, pt 1), PC1511
- (2) Ullrich; Neuro Report 1996, V7(5), P1020 MEDLINE
- L10 ANSWER 3 OF 6 MEDLINE

LINE DUPLICATE 2

AN 1999337948 MEDLINE

DN 99337948

- TI Modulation of glioma cell migration and invasion using Cl(-) and K(+) ion channel blockers.
- AU Soroceanu L; Manning T J Jr; Sontheimer H
- CS Department of Neurobiology, The University of Alabama at Birmingham, Birmingham, Alabama 35294-0021, USA.
- NC NS36692 (NINDS)
- SO JOURNAL OF NEUROSCIENCE, (1999 Jul 15) 19 (14) 5942-54. Journal code: JDF. ISSN: 0270-6474.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 199910

into

- EW 19991001
- AB Human malignant gliomas are highly invasive tumors. Mechanisms that allow glioma cells to disseminate, migrating through the narrow extracellular brain spaces are poorly understood. We recently demonstrated

expression of large voltage-dependent chloride (Cl(-)) currents, selectively expressed by human glioma cells in vitro and in situ (Ullrich et al., 1998). Currents are sensitive to several Cl(-) channel blockers, including  ${\bf chlorotoxin}$  (Ctx), (Ullrich and Sontheimer; 1996; Ullrich et al; 1996), tetraethylammonium chloride (TEA), and tamoxifen (Ransom and Sontheimer, 1998). Using Transwell migration assays, we show that blockade of glioma Cl(-) channels specifically inhibits  ${\bf tumor}$  cell migration in a dose-dependent manner. Ctx (5 microM), tamoxifen (10 microM), and TEA (1 mM) also prevented invasion of human glioma cells

fetal rat brain aggregates, used as an in vitro model to assess tumor invasiveness. Anion replacement studies suggest that permeation of chloride ions through glioma chloride channel is obligatory for cell migration. Osmotically induced cell swelling and subsequent regulatory volume decrease (RVD) in cultured glioma cells were reversibly prevented by 1 mM TEA, 10 microM tamoxifen, and irreversibly blocked by 5 microM Ctx added to the hypotonic media. Cl(-) fluxes associated with adaptive shape changes elicited by cell swelling and RVD in glioma cells were inhibited by 5 microM Ctx, 10 microM

tamoxifen, and 1 mM TEA, as determined using the Cl(-)-sensitive fluorescent dye 6-methoxy-N-ethylquinolinium iodide. Collectively, these

data suggest that chloride channels in glioma cells may enable tumor invasiveness, presumably by facilitating cell shape and cell volume changes that are more conducive to migration and invasion.

- L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2000 ACS
- AN 1998:111924 CAPLUS
- DN 128:229085
- TI Expression of voltage-activated chloride currents in acute slices of human

gliomas

- AU Ullrich, N.; Bordey, A.; Gillespie, G. Y.; Sontheimer, H.
- CS Department of Neurobiology, University of Alabama at Birmingham, Birmingham, AL, 35294, USA
- SO Neuroscience (Oxford) (1998), 83(4), 1161-1173 CODEN: NRSCDN; ISSN: 0306-4522
- PB Elsevier Science Ltd.
- DT Journal
- LA English
- AB Using whole-cell patch-clamp recordings, we identified a novel voltage-activated chloride current that was selectively expressed in glioma cells from 23 patient biopsies. Chloride currents were identified in 64% of glioma cells studied in acute slices of nine patient biopsies. These derived from gliomas of various pathol. grades. In addn., 98% of cells acutely isolated or in short-term culture from 23 patients diagnosed

with gliomas showed chloride current expression. These currents, which we

termed glioma chloride currents activated at potentials >45 mV, showed pronounced outward rectification, and were sensitive to bath application of the presumed Cl- channel specific peptide chlorotoxin (.apprx.600 nM) derived from Leiurus scorpion venom. Interestingly, low grade tumors (e.g., pilocytic astrocytomas), contg. more differentiated, astrocyte-like cells showed expression of glioma chloride currents in concert with voltage-activated sodium and potassium currents also seen in normal astrocytes. By contrast, high grade tumors (e.g., glioblastoma multiforme) expressed almost exclusively chloride currents, suggesting a gradual loss of Na+ currents and gain of Clcurrents with increasing pathol. tumor grade. To expand on the observation that these chloride currents are glioma-specific, we introduced exptl. tumors in scid mice by intracranial injection of D54MG glioma cells and subsequently recorded from tumor cells and adjacent normal glial cells in acute slices. We consistently obsd. expression of chlorotoxin-sensitive chloride channels in implanted glioma cells, but without evidence for expression of chloride channels in surrounding "normal" host glial cells, suggesting that these chloride channels are probably a glioma-specific feature. Finding of

this

novel glioma specific C1- channel in gliomas in situ and it's selective binding of **chlorotoxin** may provide a way to identify or target glioma cells in the future.

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L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2000 ACS
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- AN 1997:505749 CAPLUS
- DN 127:119322
- TI Method of diagnosing and treating gliomas
- IN Sontheimer, Harald W.; Ullrich, Nicole
- PA UAB Research Foundation, USA
- SO PCT Int. Appl., 81 pp.
- CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
		<del>-</del>		<del>_</del>	
ΡI	WO 9724619	A1	19970710	WO 1996-US20403	19961227

W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,

SE

CA 2249351 AA 19970710 CA 1996-2249351 19961227 AU 9722399 A1 19970728 AU 1997-22399 19961227 EP 953153 A1 19991103 EP 1996-946129 19961227

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI US 1995-9283 19951227 WO 1996-US20403 19961227

AB The present invention relates generally to the fields of cell physiol., neurol. and neuro-oncol. More specifically, the present invention relates

to a novel method of detection of the membrane protein "glioma chloride channel" for use as a specific tumor
marker for the diagnosis and treatment of gliomas and meningiomas. The invention describes the expression of this chloride conductance with unique properties that selectively characterizes tumor-derived cells of glial origin. Whole-cell patch-clamp techniques were used to characterize the biophys. and pharmacol. properties of chloride channels in primary cultures and acutely isolated cells from biopsies of human astrocytomas and established cell lines.

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2000 ACS

AN 1996:325861 CAPLUS

DN 125:48543

TI Biophysical and pharmacological characterization of chloride currents in human astrocytoma cells

AU Ullrich, Nicole; Sontheimer, Harald

CS Neurobiology Research Center, University Alabama Birmingham, Birmingham, AL, 35294, USA

SO Am. J. Physiol. (1996), 270(5, Pt. 1), C1511-C1521 CODEN: AJPHAP; ISSN: 0002-9513

DT Journal

LA English

AB Expression of voltage-activated ion channels was studied in primary cultures from seven freshly resected human primary brain tumors and in an established human astrocytoma cell line, STTG1. Astrocytoma cells consistently expressed voltage-dependent outwardly rectifying currents. Currents activated at potentials >45 mV and showed outward transients on termination of voltage steps. Currents reversed at the Clequil. potential, suggesting that they were largely carried by Cl-. Altering extracellular K+ or Na+ concn. did not alter currents; neither did replacement of intracellular K+ by Cs+ or intracellular Na+ by N-methyl-D-glucosamine. Anion-substitution expts. suggest the following permeability sequence, detd. from shifts in tail current reversal potential: I- > NO3- > Br- > Cl- > acetate > isethionate > F- >

Currents were sensitive to the Cl- channel blockers chlorotoxin, 4,4'-diisothiocyanostilbene-2,2'-disulfonic acid (DIDS), and 4,4'-dinitrostilbene-2,2'-disulfonic acid (DNDS), with chlorotoxin being most effective, yielding >80% block at 590 nM. DIDS (100 .mu.M)

and

DNDS (100 .mu.M) reduced currents by 33.5 and 38.2%, resp. Currents were also sensitive to Zn2+ (100 .mu.M, 47% block) and Cd2+ (25 .mu.M, 42% block). Reducing extracellular Ca2+ concn. decreased outward currents by 58% and almost completely eliminated transients, suggesting that Cl-currents are Ca2+ dependent. Cl- channel block resulted in altered cell proliferation as detd. by [3H]thymidine incorporation, suggesting that

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(FILE 'HOME' ENTERED AT 17:37:50 ON 20 JUN 2000)
     FILE 'MEDLINE, BIOSIS, CAPLUS, USPATFULL' ENTERED AT 17:38:38 ON 20 JUN
     2000
L1
           8621 S NEUROECTODERM?
L2
        1342108 S ANTIBODY OR ANTIBODIES
L3
             56 S CHLOROTOXIN?
           8267 S CHLORIDE CHANNEL
T.4
L5
        2525715 S TUMOR? OR CANCER? OR NEOPLAS?
1.6
             20 S L3 AND L4
            454 S L2 AND L4
T.7
              9 S L6 AND L5
1.8
L9
            108 S L7 AND L5
              6 DUP REM L8 (3 DUPLICATES REMOVED)
L10
=> s 19 and 11
             3 L9 AND L1
L11
=> dup rem 111
PROCESSING COMPLETED FOR L11
              3 DUP REM L11 (0 DUPLICATES REMOVED)
=> d 112 1-3 bib abs
L12 ANSWER 1 OF 3 USPATFULL
       2000:37945 USPATFULL
AN
       Hydroxy and ether-containing oxyalkylene esters and uses thereof
ΨT
      Nudelman, Abraham, Rehovot, Israel
IN
      Rephaeli, Ada, North Caldwell, NJ, United States
      Mor Research Applications, Ltd., Givat Shmuel, Israel (non-U.S.
PA
       corporation)
       Beacon Laboratories, Inc., Phoenix, MD, United States (U.S.
corporation)
       Bar-Ilan University, Ramat-Gan, Israel (non-U.S. corporation)
PΙ
       US 6043389 20000328
      US 1997-814224 19970311 (8)
ΑI
      Utility
DΤ
EXNAM Primary Examiner: Reamer, James H.
LREP
      Kenyon & Kenyon
CLMN
      Number of Claims: 4
ECL
      Exemplary Claim: 1
       4 Drawing Figure(s); 2 Drawing Page(s)
DRWN
LN.CNT 1117
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      This invention relates to compositions for and methods of treating,
AΒ
       preventing or ameliorating cancer and other proliferative
       diseases as well as methods of inducing wound healing, treating
       cutaneous ulcers, treating gastrointestinal disorders, treating blood
       disorders such as anemias, immunomodulation, enhancing recombinant gene
       expression, treating insulin-dedendent patients, treating cystic
       fibrosis patients, inhibiting telomerase activity, treating
       virus-associated tumors, especially EBV-associated
     tumors, augmenting expression of tumor suppressor
       genes, inducing tolerance to antigens, or treating, preventing or
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ameliorating protozoan infection or inhibiting histone deacetylase in cells. The compositions of the invention are to and the methods of the invention use hydroxy and ether-containing oxyalkylene esters.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L12 ANSWER 2 OF 3 USPATFULL
       2000:24635 USPATFULL
ΝA
       Oxyalkylene phosphate compounds and uses thereof
TΙ
       Nudelman, Abraham, Rehovot, Israel
IN
       Rephaeli, Ada, North Caldwell, NJ, United States
       Bar-Ilan Research & Development Co., Ltd., Ramat-Gan, Israel (non-U.S.
PA
       corporation)
       Mor Research Applications Ltd., Givat Shmuel, Israel (non-U.S.
       corporation)
PΙ
       US 6030961 20000229
ΑI
       US 1997-814386 19970311 (8)
DT
       Utility
EXNAM
      Primary Examiner: Raymond, Richard L.
       Kenyon & Kenyon
LREP
CLMN
       Number of Claims: 52
ECL
       Exemplary Claim: 1
DRWN
       7 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1482
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention relates to compositions for and methods of treating,
       preventing or ameliorating cancer and other proliferative
       diseases as well as methods of inducing wound hearing, treating
       cutaneous ulcers, treating gastrointestinal disorders, treating blood
       disorders such as anemias, immunomodulation, enhancing recombinant gene
       expression, treating insulin-dependent patients, treating cystic
       fibrosis patients, inhibiting telomerase activity, treating
       virus-associated tumors, especially EBV-associated
     tumors, modulating gene expression and in particular, augmenting
       expression of tumor suppressor genes, inducing tolerance to
       antigens, treating, preventing or ameliorating protozoan infection, or
       inhibiting histone deacetylase in cells. The compositions of the
       invention are to and the methods of the invention use oxyalkalene
       phosphate compounds.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 3 OF 3 USPATFULL
       1999:96406 USPATFULL
AN
ΤI
       Therapeutic augmentation of oxyalkylene diesters and butyric acid
       derivatives
       Rephaeli, Ada, North Caldwell, NJ, United States
IN
       Beacon Laboratories, Inc., Phoenix, MD, United States (U.S.
PΑ
corporation)
PΙ
       US 5939455 19990817
       US 1997-814222 19970311 (8)
ΑI
DT
       Utility
EXNAM Primary Examiner: Weddington, Kevin E.
LREP
       Kenyon & Kenyon
CLMN
       Number of Claims: 63
ECL
       Exemplary Claim: 1
DRWN
      No Drawings
LN.CNT 1545
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention provides a method of augmenting the therapeutic activity
AΒ
       of an oxyalkylene-containing compound, butyric acid, a butyric acid
salt
       or butyric acid derivative by administering an inhibitor of
       .beta.-oxidation of fatty acids to a patient or to host cells.
       Pharmaceutical compositions are also included.
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(FILE 'HOME' ENTERED AT 17:37:50 ON 20 JUN 2000) FILE 'MEDLINE, BIOSIS, CAPLUS, USPATFULL' ENTERED AT 17:38:38 ON 20 JUN 2000 L18621 S NEUROECTODERM? 1342108 S ANTIBODY OR ANTIBODIES L2 L3 56 S CHLOROTOXIN? 8267 S CHLORIDE CHANNEL L4L5 2525715 S TUMOR? OR CANCER? OR NEOPLAS? L6 20 S L3 AND L4 L7 454 S L2 AND L4 9 S L6 AND L5 L8L9 108 S L7 AND L5 6 DUP REM L8 (3 DUPLICATES REMOVED) L10 L11 3 S L9 AND L1 L12 3 DUP REM L11 (0 DUPLICATES REMOVED) => s 11 and 12 and 14 3 L1 AND L2 AND L4 L13 => d 113 1-3 bib abs kwic L13 ANSWER 1 OF 3 USPATFULL 2000:37945 USPATFULL AN ΤI Hydroxy and ether-containing oxyalkylene esters and uses thereof IN Nudelman, Abraham, Rehovot, Israel Rephaeli, Ada, North Caldwell, NJ, United States Mor Research Applications, Ltd., Givat Shmuel, Israel (non-U.S. PA corporation) Beacon Laboratories, Inc., Phoenix, MD, United States (U.S. corporation) Bar-Ilan University, Ramat-Gan, Israel (non-U.S. corporation) US 6043389 20000328 PΙ ΑI US 1997-814224 19970311 (8) Utility DTEXNAM Primary Examiner: Reamer, James H. Kenyon & Kenyon LREP CLMN Number of Claims: 4 ECL Exemplary Claim: 1 4 Drawing Figure(s); 2 Drawing Page(s) DRWN LN.CNT 1117 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AB This invention relates to compositions for and methods of treating, preventing or ameliorating cancer and other proliferative diseases as well as methods of inducing wound healing, treating cutaneous ulcers, treating gastrointestinal disorders, treating blood disorders such as anemias, immunomodulation, enhancing recombinant gene expression, treating insulin-dedendent patients, treating cystic fibrosis patients, inhibiting telomerase activity, treating virus-associated tumors, especially EBV-associated tumors, augmenting expression of tumor suppressor genes, inducing tolerance to antigens, or treating, preventing or ameliorating protozoan infection or inhibiting histone deacetylase in cells. The compositions of the invention are to and the methods of the invention use hydroxy and ether-containing oxyalkylene esters.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
SUMM
       . . . ovarian cancers, pancreatic cancers, hepatocarcinomas,
prostate
       cancers, squamous carcinomas, other dermatologic malignancies,
       teratocarcinomas, T-cell lymphomas, lung tumors, gliomas,
       neuroblastomas, peripheral neuroectodermal tumors,
       rhabdomyosarcomas, and prostate tumors and other solid tumors. It is
       also possible that compounds of Formula I have anti-proliferative.
SUMM
          . . are not limited to, thalassemias, sickle cell anemias,
       infectious anemias, aplastic anemias, hypoplastic and hypoproliferative
       anemias, sideroblastic anemias, myelophthisic anemias, antibody
       -mediated anemias, anemias due to chronic diseases and
       enzyme-deficiencies, and anemias due to blood loss, radiation therapy
       and chemotherapy. In this.
SUMM
       . . agents of the invention for the above method include, but are
       not limited to, cytokines, interleukins, anti-cancer agents,
       chemotherapeutic agents, antibodies, conjugated
     antibodies, immune stimulants, antibiotics, hormone antagonists,
       and growth stimulants. The compounds of the invention can be
       administered prior to, after or.
SUMM
       . . . or ameliorating symptoms in cystic fibrosis patients by
       administering an amount of a compound of Formula I effective to enhance
     chloride channel expression.
       . . . recombinant gene expression; to modulate gene expression; to
DETD
       augment expression of tumor suppressor genes; to enhance insulin
       expression; to enhance chloride channel expression,
       to induce tolerance to an antigen; to treat, prevent or ameliorate
      protozoan infection; or to inhibit histone deacetylase in.
       . . differentiating agents. For example, the pharmaceutical agent
DETD
      can be a cytokine, an interleukin, an anti-cancer agent, a
       chemotherapeutic agent, an antibody, a conjugated
     antibody, an immune stimulant, an antibiotic, a hormone
       antagonist or a growth stimulant. The pharmaceutical agent can also be
a
      cytotoxic.
       . . al., Md. Carcin. 3:350-362, 1990). Casein detection can be
DETD
done
      by histochemical staining of breast cancer cells using a human
     antibody to human casein as described by Cheung et al., J. Clin.
      Invest. 75:1722-1728, which is incorporated by reference in its.
DETD
       . . . prepared and the cells are fixed with ethanol. Fixed cells are
       reacted overnight at 4.degree. C. with the primary monoclonal
     antibody, anti-Bcl-2 at a dilution of 1:50. Staining is
      completed to visualize antibody binding, for example, using
      Strep A-B Universal Kit (Sigma) in accordance with the manufacturer's
       instructions. Identically-treated cells which received no primary
     antibody can serve as a non-specific binding control. Commercial
      kits are also available and can be used for detecting apoptosis, for.
      The level of CD11b was measured on HL-60 cells by flow cytometry using
DETD
а
      monoclonal antibody (MAb) against CD11b in a standard indirect
       immunofluorescence assay. Cells were cultured for 6 days with the
       indicated concentration of.
L13 ANSWER 2 OF 3 USPATFULL
      2000:24635 USPATFULL
ΑN
      Oxyalkylene phosphate compounds and uses thereof
ΤI
      Nudelman, Abraham, Rehovot, Israel
IN
      Rephaeli, Ada, North Caldwell, NJ, United States
      Bar-Ilan Research & Development Co., Ltd., Ramat-Gan, Israel (non-U.S.
PA
      corporation)
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Mor Research Applications Ltd., Givat Shmuel, Israel (non-U.S.

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corporation)
ΡI
       US 6030961 20000229
ΑI
       US 1997-814386 19970311 (8)
DT
       Utility
EXNAM
       Primary Examiner: Raymond, Richard L.
LREP
       Kenyon & Kenyon
CLMN
       Number of Claims: 52
ECL
       Exemplary Claim: 1
DRWN
       7 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1482
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention relates to compositions for and methods of treating,
       preventing or ameliorating cancer and other proliferative diseases as
       well as methods of inducing wound hearing, treating cutaneous ulcers,
       treating gastrointestinal disorders, treating blood disorders such as
       anemias, immunomodulation, enhancing recombinant gene expression,
       treating insulin-dependent patients, treating cystic fibrosis patients,
       inhibiting telomerase activity, treating virus-associated tumors,
       especially EBV-associated tumors, modulating gene expression and in
       particular, augmenting expression of tumor suppressor genes, inducing
       tolerance to antigens, treating, preventing or ameliorating protozoan
       infection, or inhibiting histone deacetylase in cells. The compositions
       of the invention are to and the methods of the invention use
oxyalkalene
       phosphate compounds.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      . . . ovarian cancers, pancreatic cancers, hepatocarcinomas,
prostate
       cancers, squamous carcinomas, other dermatologic malignancies,
       teratocarcinomas, T-cell lymphomas, lung tumors, gliomas,
       neuroblastomas, peripheral neuroectodermal tumors,
       rhabdomyosarcomas, and prostate tumors and other solid tumors. It is
       also possible that compounds of Formula I as defined. .
SUMM
       . . . are not limited to, thalassemias, sickle cell anemias,
       infectious anemias, aplastic anemias, hypoplastic and hypoproliferative
       anemias, sideroblastic anemias, myelophthisic anemias, antibody
       -mediated anemias, anemias due to chronic diseases and
       enzyme-deficiencies, and anemias due to blood loss, radiation therapy
       and chemotherapy. In this.
       . . agents of the invention for the above method include but are
SUMM
      not limited to, cytokines, interleukins, anti-cancer agents,
       chemotherapeutic agents, antibodies, conjugated
     antibodies, immune stimulants, antibiotics, hormone antagonists,
       and growth stimulants. The compounds of the invention can be
       administered prior to, after or.
       . . . in cystic fibrosis patients by administering an amount of a
SUMM
       compound of Formula I as defined above effective to enhance
    chloride channel expression.
       . . . immune response; to enhance gene expression; modulate or
DETD
       augment expression of tumor suppressor genes; to enhance insulin
       expression; to enhance chloride channel expression;
       to induce tolerance to an antigen; to treat, prevent or ameliorate
      protozoan infection; or to inhibit histone deacetylase in.
DETD
      . . . differentiating agents. For example, the pharmaceutical agent
      can be a cytokine, an interleukin, an anti-cancer agent, a
       chemotherapeutic agent, an antibody, a conjugated
    antibody, an immune stimulant, an antibiotic, a hormone
      antagonist or a growth stimulant. The pharmaceutical agent can also be
      cytotoxic.
        . . al., Md. Carcin. 3:350-362, 1990). Casein detection can be
DETD
done
      by histochemical staining of breast cancer cells using a human
```

antibody to human casein as described by Cheung et al., J. Clin.

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Invest. 75:1722-1728, which is incorporated by reference in its. . .
DETD
       . . . prepared and the cells are fixed with ethanol. Fixed cells are
      reacted overnight at 4.degree. C. with the primary monoclonal
     antibody, anti-Bcl-2 at a dilution of 1:50. Staining is
       completed to visualize antibody binding, for example, using
      Strep A-B Universal Kit (Sigma) in accordance with the manufacturer's
      instructions. Identically-treated cells which received no primary
     antibody can serve as a non-specific binding control. Commercial
      kits are also available and can be used for detecting apoptosis, for.
      The level of CD11b was measured on HL-60 cells by flow cytometry using
DETD
      monoclonal antibody (MAb) against CD11b in a standard indirect
      immunofluorescence assay. Cells were cultured for three or six days
with
      the indicated.
CLM
      What is claimed is:
         selected from the group consisting of a cytokine, an interleukin, an
      anti-cancer agent of anti-neoplastic agent, a chemotherapeutic agent,
an
    antibody, a conjugated antibody, an immune stimulant,
      antibiotic, a hormone antagonist and a growth stimulant.
L13 ANSWER 3 OF 3 USPATFULL
      1999:96406 USPATFULL
      Therapeutic augmentation of oxyalkylene diesters and butyric acid
ΤI
IN
      Rephaeli, Ada, North Caldwell, NJ, United States
      Beacon Laboratories, Inc., Phoenix, MD, United States (U.S.
corporation)
      US 5939455 19990817
      US 1997-814222 19970311 (8)
ΑI
EXNAM Primary Examiner: Weddington, Kevin E.
      Kenyon & Kenyon
LREP
      Number of Claims: 63
CLMN
      Exemplary Claim: 1
ECL
      No Drawings
DRWN
LN.CNT 1545
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      This invention provides a method of augmenting the therapeutic activity
AΒ
      of an oxyalkylene-containing compound, butyric acid, a butyric acid
salt
      or butyric acid derivative by administering an inhibitor of
       .beta.-oxidation of fatty acids to a patient or to host cells.
      Pharmaceutical compositions are also included.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
               pharmaceutical compositions further containing a
      . . .
pharmaceutical
      agent selected from a cytokine, an interleukin, an anti-cancer agent, a
      chemotherapeutic agent, an antibody, a conjugated
    antibody, an immune stimulant, an antibiotic, a hormone
      antagonist, a growth stimulant, an antiviral agent or a cytotoxic
agent.
       . . . ovarian cancers, pancreatic cancers, hepatocarcinomas,
DETD
prostate
      cancers, squamous carcinomas, other dermatologic malignancies,
      teratocarcinomas, T-cell lymphomas, lung tumors, gliomas,
      neuroblastomas, peripheral neuroectodermal tumors,
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rhabdomyosarcomas, and prostate tumors and other solid tumors. It is also possible that compounds of the invention have anti-proliferative.

DETD

а

. agents of the invention for the above method include, but are not limited to, cytokines, interleukins, anti-cancer agents, chemotherapeutic agents, antibodies, conjugated

antibodies, immune stimulants, antibiotics, hormone antagonists, and growth stimulants. The .beta.-oxidation inhibitor and compounds of the invention can be administered prior.

. . . are not limited to, thalassemias, sickle cell anemias, DETD infectious anemias, aplastic anemias, hypoplastic and hypoproliferative anemias, sideroblastic anemias, myelophthisic anemias, antibody -mediated anemias, anemias due to chronic diseases and enzyme-deficiencies, and anemias due to blood loss, radiation therapy and chemotherapy. In this.

In yet another embodiment, the therapeutic activity is effective to DETD enhance chloride channel expression in a cystic fibrosis patient.

DETD . . . recombinant gene expression; to modulate gene expression; to augment expression of tumor suppressor genes; to enhance insulin expression; to enhance chloride channel expression; to induce tolerance to an antigen; to treat, prevent or ameliorate protozoan infection; or to inhibit histone deacetylase in. . .

DETD . . . as differentiating agents. Further, the pharmaceutical agent can be a cytokine, an interleukin, an anti-cancer agent, a chemotherapeutic agent, an antibody, a conjugated

antibody, an immune stimulant, an antibiotic, a hormone antagonist or a growth stimulant. The pharmaceutical agent can also be

cytotoxic. DETD . . al., Md. Carcin. 3:350-362, 1990). Casein detection can be done

by histochemical staining of breast cancer cells using a human antibody to human casein as described by Cheung et al., J. Clin. Invest. 75:1722-1728, which is incorporated by reference in its.

. . prepared and the cells are fixed with ethanol. Fixed cells are DETD reacted overnight at 4.degree. C. with the primary monoclonal antibody, anti-Bcl-2 at a dilution of 1:50. Staining is completed to visualize antibody binding, for example, using Strep A-B Universal Kit (Sigma) in accordance with the manufacturer's instructions. Identically-treated cells which received no primary antibody can serve as a non-specific binding control. Commercial kits are also available and can be used for detecting apoptosis, for.

What is claimed is:

. from the group consisting of a cytokine, an interleukin, an anti-cancer agent or an anti-neoplastic agent, a chemotherapeutic agent,

an antibody, a conjugated antibody, an immune stimulant, an antibiotic, a hormone antagonist or a growth stimulant.

36. The method of claim 1 wherein said therapeutic activity is effective

to enhance chloride channel expression in a cystic fibrosis patient.

a pharmaceutical agent selected from the group consisting of a cytokine, an interleukin, an anti-cancer agent, a chemotherapeutic agent, an antibody, a conjugated antibody, an immune stimulant, an antibiotic, a hormone antagonist, a growth stimulant, an antiviral agent and a cytotoxic agent.